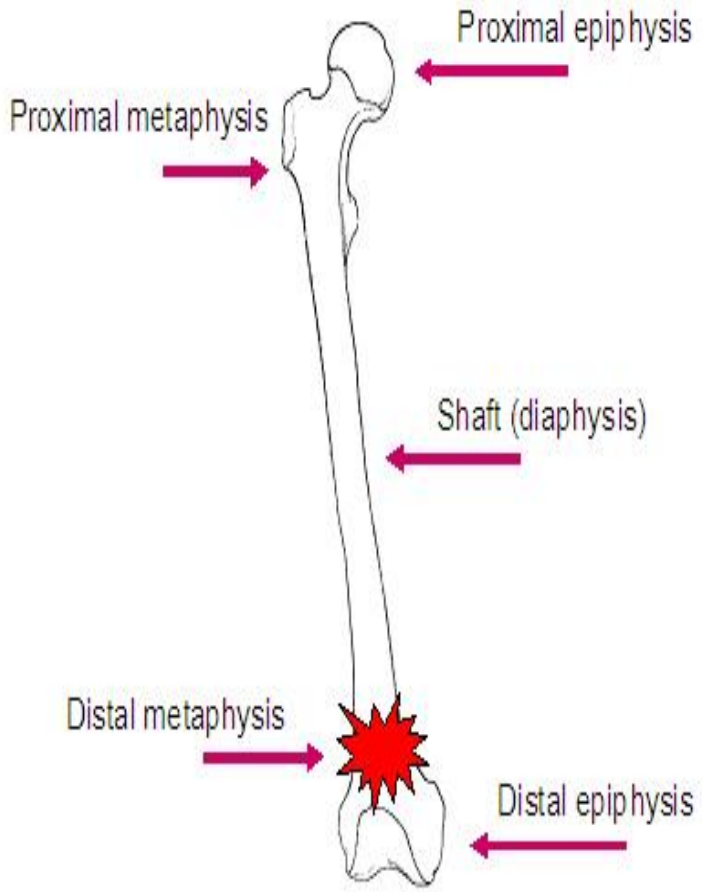
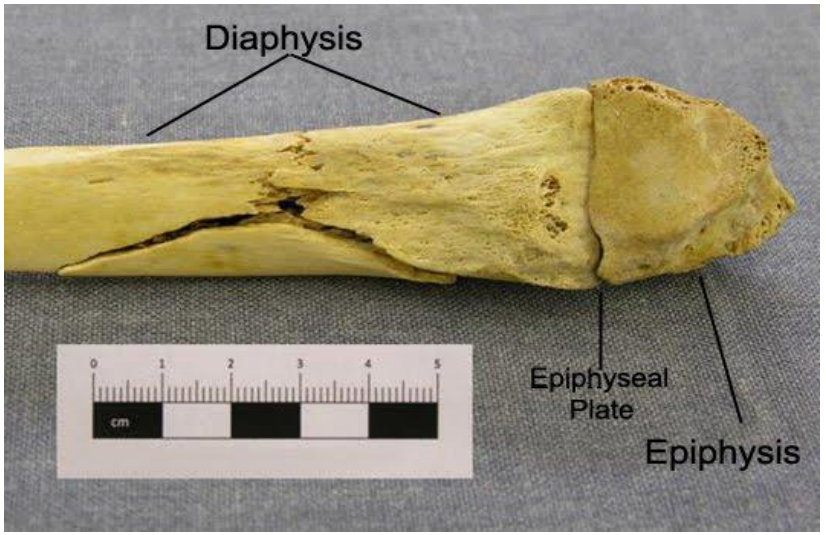
Microbiology of Bone and Joint Infections

MUSCULOSKELETAL BLOCK
PROF.HANAN HABIB
DEPARTMENT OF PATHOLOGY
KSU

Introduction

- Bone & joint infections may exist separately or together.
- Both are more common in infants and children
- Usually caused by **blood** borne spread ,but can result from **local** trauma or spread from **contiguous soft tissue infection.**
- Often associated with **foreign body** at the primary wound site.
- If not treated lead to devastating effect


Proximal epiphysis
Proximal metaphysis
Shaft (diaphysis)
Distal metaphysis
Distal epiphysis


Diaphysis
Epiphyseal Plate
Epiphysis

What is Acute Osteomyelitis

- Acute osteomyelitis is acute infectious process of the bone and bone marrow .
- Can have a short duration
  - few days for hematogenously acquired infection
- last several weeks to months
  - if secondary to contiguous focus of infection)

- In association with peripheral vascular disease
  - diabetes mellitus ,severe atherosclerosis, vasculitis

How they reach	Risk Group	
Primary Hematogenous route (Metaphysis of long bones)	Children common Adult less common (quiescent from childhood) -S. Aureus septic arthritis –diaphysis -Vertebral- GU infection -Candida –Venous Catheter	Infant S.aureus, group B streptococci, E.coli.
		Children S.aureus, group A streptococci, H.influenzae.
Contiguous soft tissue focus	Post operative infection, contaminated open fracture, soft tissue infection , puncture wounds	Gram positive cocci, Gram negative bacilli, anaerobes, and poly-microbial infection.
Special clinical situations	Prosthesis	Coagulas -negative staphylococci, Propionebacterium, and S.aureus in foreign body infections
	Nosocomial infections and IV drug use	Enterobacteriacea and Pseudomonas
	Fist injuries, and diabetic foot and dicubitus ulcers,	Streptococci and anaerobes
	in sickle cell patients	Salmonella or S. pneumoniae
	Human/ animal bites;	Eikenella, Pasturella multocida
	AIDS.	M.tuberculosis or M. avium

Patient Presentation

- Systemic manifestations occurs in less than 50% of patients.
- **Acute onset of bone pain, fever with rigors and diaphoresis.**
- Symptoms usually of less than 3 week's duration.
- **Local signs** : soft tissue swelling, erythema, warmth, point tenderness, percussion tenderness over the vertebral body & limited mobility of the involved extremity.

Differential diagnosis

- Primary and metastatic bone malignancies
- Trauma
- Acute rheumatic arthritis
- Hemarthrosis
- Ewing sarcoma
- Vertebral compression fracture.

Diagnosis

Laboratory	Radiological
-CBC diff -Leukocytosis may or may not occur -Erythrocyte sedimentation rate (ESR) elevated, but could be normal as well	-X-ray : normal early in disease, soft tissue swelling , subperiosteal elevation seen early. Bone destruction changes seen by 2-4 weeks.
-Blood culture. -Aspiration of overlying abscess if blood cultures are negative	-MRI highly sensitive & specific. Preferred for vertebral osteomyelitis and cases associated with contiguous foci of infection or peripheral vascualr disease.
	-CT Scan used as alternative of MRI.
	-Technetium bone scan, Gallium –and Indium -111-labelled WBC scan (detection within 3 days of onset). Maximum effect to rule out osteomyelitis.

Organisms	Antibiotics	Duration/Surgery/complication and follow up
MSSA:	Cloxacillin, cefazolin or Clindamycin .	Early treatment is critical Treat for 2-4 weeks parenteral followed by oral therapy for a total of at least 6 weeks. Surgery for neurological complications, para-vertebral abscess & hip joint involvement. Complications: septicemia, metastatic abscesses, septic arthritis, chronic osteomyelitis, loss of limb ,or paravertebral abscess. Monthly ESR for 3 months and at 6 months useful to document treatment. Cases due to contiguous source more difficult to eradicate .Relapse common (50%) , surgery indicated.
MRSA:	Vancomycin followed by Clindamycin, Linezolid, or TMP-SMX	
Polymicrobial infection:	Ampicillin-Sulbactam, Piperacillin-Tazobactam or Quinolone with Metronidazole.	
S.epidermidis:	Vancomycin and Rifampicin	
Enterobacteriaca e:	Ceftriaxone	
Other Gram negative bacilli:	Quinolones	
P. aeruginosa:	Cefepime, Meropenem, or Piperacillin +/- Aminoglycoside.	
Anaerobes:	Metronidazole or Clindamycin	

Chronic Osteomyelitis

- A chronic infection of the bone and bone marrow usually secondary to inadequately treated or relapse of acute osteomyelitis.
- Management difficult , prognosis poor.
- Infection may not completely cured.
- May recur many years, decades, after initial episode.
- Most infections are secondary to a contiguous focus or peripheral vascular disease;
- chronic infection due hematological spread is rare.
- TB and fungal osteomyelitis clinically have indolent “chronic” course.

Etiology, Epidemiology & Risk factors

General risk factors:

1. Penetrating trauma
2. Prosthetic devices
3. Animal bites
4. IV drug use

Host risk factors:

1. Peripheral vascular disease
2. Peripheral neuropathy
3. Sickle cell disease
4. Diabetes mellitus
5. Immunocompromised states.

Extent of disease and outcome depends on general nutritional status of involved tissues, degree of bone necrosis, virulence of pathogen.

Causative Agents

The most common pathogen	Other microorganisms	Decubitus ulcers and diabetic foot infections.
S.aureus	S.epidermidis,enterococci ,streptococci,Enterobacte ricae,Pseudomonas, Acinetobacter spp., anaerobes (Bacteroides, anaerobic streptococci, Clostridium)	Polymicrobial infection common

In immunosuppressed patients.

Mycobacteria Tuberculosis (MTB)

- *MTB* osteomyelitis
  - Primarily results from hemtogenous spread from lung foci
  - or
  - As an extension from a caseating lymph bone (50% in spine).

Fungi

- Hematogenous osteomyelitis due to fungi eg.
  - *Candida* spp.,
  - *Histoplasma*
  - *capsulatum,*
  - *Aspergillus* spp
  - Other fungi may occur.

Clinical presentation and DD

Patient Presentation	Differential Diagnosis
• Acute symptoms and systemic manifestations are uncommon. • Sinus tract • Persistent wound drainage • Chronic non-healing ulcer • Local signs may be absent except during acute exacerbation. • Overlying skin may be scarred and adherent to the involved bone.	• Osteoid osteoma • Osteosarcoma • Secondary bony metastases • Paget's disease of the bone • Gout

Diagnosis

Laboratory

- WBC normal, ESR elevated but not specific.
- Blood culture not very helpful- because as bacteremia rare.
- **Definite microbiological diagnosis by culture of bone biopsy or FNA & Histological examination)**
- **Surgery for diagnosis and therapeutic purposes**
- Wound /sinus culture not reliable. Isolation of MRSA or vancomycin resistant enterococci should initiate infection control measures.

Radiological

- Radiologic changes complicated by the presence of bony abnormalities
- **MRI helpful for diagnosis and evaluation of extent of disease.**
- Combined bone scan and Indium WBC scan.

Treatment and Management

Surgical

- Extensive surgical debridement with antibiotic therapy. Parenteral antibiotics for 3-6 weeks followed by long term oral suppressive therapy.
- Some patients may require life long antibiotic ,others for acute exacerbations.
- Other bacteria treat as acute osteomyelitis.

Medical

Organisms	Antibiotics
MSSA:	parenteral cloxacillin followed by oral treatment
MRSA & S.epidermidis:	Vancomycin (with added Rifampicin) then oral Clindamycin or TMP-SMX.
TB	4 drugs : INH,RIF ,Pyrazinamide & Ethambutol for 2 ms followed by RIF + INH for additional 4 ms.

Complications & Prognosis

Complications:

- Recurrence
- Loss of limb
- Pathological fractures
- Primary epidermoid carcinoma of sinus tract
- Malignant histocytoma
- Secondary amyloidosis
- Lymphoma & multiple myeloma(rare)

Prognosis

- Relapses are frequent

Blood culture & Bone images and cases

Arthritis

- **Infectious Arthritis** is inflammation of the joint space secondary to infection.
- Generally affects a single joint and result in suppurative inflammation.
- Hematogenous seeding of joint is most common.
- Pain, swelling, limitation of movement common symptoms
- Diagnosis by arthocentesis to obtain synovial fluid for analysis
- Gram stain, culture & sensitivity
- Drainage & antimicrobial therapy important management.

Pathophysiology & Risk factors

Pathophysiology

- Results from introduction of organisms into joint space as a results of bacteremia or fungemia from infection at other body sites.
- Occasionally results from direct trauma, procedures (arthroscopy) or from contiguous soft tissue infection.

Risk factors

- Age
- Diabetes
- Immunosuppresion
- IV drug use
- CV catheters
- Prior joint damage (rheumatoid arthritis) or procedure (arthroscopy)
- H/O sexually transmitted diseases.

Etiology

Common Organisms

- S.aureus is most common cause.
- Gonococcal infection most common cause in young, sexually active adults
- Caused by *Neisseria gonorrheae* leads to disseminated infection secondary to urethritis/cervicitis.
- Nongonococcal arthritis occurs in older adults.

Other Organisms

- Streptococci and aerobic Gram negative bacilli.
- Lyme disease in endemic areas.
- Chronic arthritis may be due to MTB or fungi in Immunocopramized
- IV drug user Sternoclavecular or Sacroilliac due to P.aeruginosa

Patient Presentation

Gonococcal arthritis

1. **Early disease**: fever, rash, tenosynovitis (especially of hands, wrists), polyarthralgia resulting from non-suppurative arthritis.
2. **Late disease**: monoarticular, suppurative arthritis.

Non-gonococcal arthritis

- Monoarthicular suppurative

Arthritis

- Knee and wrist are themost common, fever and pain
- Swollen and tender join with Joint effusion and limitation of joint movement

Differential Diagnosis

- Crystal –induced arthritis
  - Gout, pseudogout
- Noninfectious inflammatory arthritis
  - Acute rheumatoid arthritis
- Reactive arthritis
  - Reiter syndrome, acute rheumatic fever
- Trauma
- Viral arthritis
  - Parvovirus B19, Hepatitis B virus.

Samples	Tests
Arthrocentesis should be done as soon as possible;	1-Synovial fluid is cloudy and purulent 2- Leukocyte count generally > 50,000/mm3,with > 75 % PMN 3- Gram stain and culture are positive in >90% of cases 4-Exclude crystal deposition arthritis or noninfectious inflammatory arthritis.
Blood cultures - Culture of skin lesions can be performed	indicated
Cervix, urethra, rectum & pharynx Swab or urine	If gonococcal infection suspected for N.gonorrheae for culture and DNA testing for N.gonorrheae.
Skin Rash	Can be culture
History/examination to exclude systemic illness. Note H/O tick exposure in endemic areas and sexual contact.	

Treatment & Management

Nongonococcal infectiuos arthritis:

1. MSSA: Cloxacillin or Cefazolin
2. MRSA: Vancomycin
3. Streptococci: Penicillin or Ceftriaxone or Cefazolin
4. *Enterobacetriacae*: Ceftriaxone or Fluroquinolone
5. *Pesudomonas*: Piperacillin and Aminoglycoside
6. Animal bite : Ampicillin-Sulbactam
7. Lyme disease arthritis: Doxycycline for 1 month.

Gonococcal arthritis:

- IV Ceftriaxone (or Ciprofloxacin or Ofloxacin) then switch to oral Quinolone or Cefixime for 7-10 days.

Change the antibiotics according to sensitivity, Arthrocentesis can repeated and Surgery rarely required

Prognosis & Complications

Prognosis

- Gonococcal arthritis has an excellent outcome
- Risk factors for long –term adverse sequellae include:
  - Age
  - Prior rheumatoid arthritis
  - Poly-articular joint involvement
  - Hip or shoulder involvement
  - Virulent pathogens
  - Delayed initiation or response to therapy

Complications

- Nongonococcal arthritis: can result in scarring with limitation of movement, ambulation is affected in 50% of cases.

Arthritis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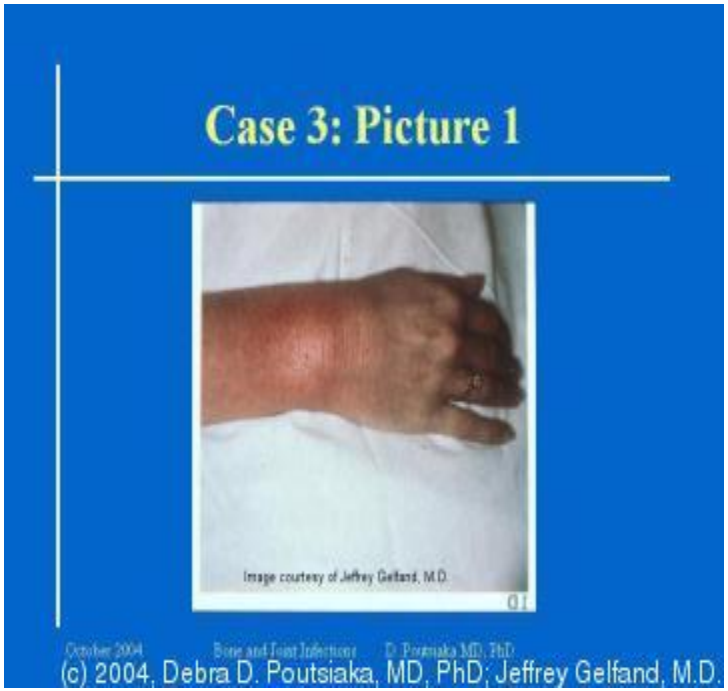
Case 3: Picture 1
Image courtesy of Jeffrey Gelfand, M.D.
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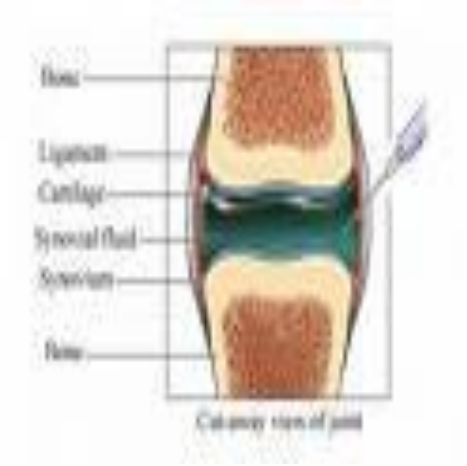
Joint Aspiration (Arthrocentesis)

Joint aspiration



Cut-away view of joint

TABLE FINDINGS IN SYNOVIAL FLUID IN VARIOUS FORMS OF ARTHRITIS

Laboratory Test	Normal	Septic Bacterial Arthritis	Trauma, Degenerative Joint Disease	Rheumatic Arthritis Gout
Clarity and color	Clear	Opaque, yellow to green	Clear, yellow	Translucent or opalescent
Viscosity	High	Variable	High	Low
White blood cells/mm^3	<200	25,000-100,000	200-2000	2000-20,000
Polymorphonuclear cells (%)	<25	>75	25-50	≥50
Glucose level (relative to ıeous blood glucose level)	Nearly equal	<25%	Nearly equal	50+80%

Infections of Joint Prosthesis

- 1-5% of total joint replacement.
- Most infections occurs within 5 years of joint replacement.
- Often caused by skin flora
- Diagnostic aspiration of joint fluid necessary
- Result in significant morbidity and health care costs.
- Successful outcomes results from multidisciplinary approach.

Etiology, Epidemiology& Risk factors

- Results from contamination during surgery or post op. wound infection adjacent to the prosthesis.
- Factors delay healing (hematoma, ischemia)
- Occasionally result from bacteremia
- Prosthesis & bone cement predispose to infection
- Occurs at the prosthesis-bone interface
- Bacteria adhere to biomaterials and develop a biofilm that protect them from host defenses and antimicrobial agents.
- Mostly caused by coagulase negative staph., or *S.aureus*.

- Occasional pathogens: streptococci, enterococci ,and anaerobes
- Usually single pathogen ,occasionally polymicrobial
- **Risk factors**: H/O superficial wound infection, post surgical complications, underlying illness, any source of bacteremia.
- **Differential diagnosis**:

Aseptic loosening or dislocation of prosthetic joint

Prosthetic debris induced cynovitis & hemarthrosis

Patient Presentation

- Subacute onset
- *S.aureus*, streptococci,Gram negative rods can cause acute ,rapidly progressive infection
- Joint pain ,swelling most common
- Fever with acute ,early postsurgical infections
- Cellulitis, cutaneous wound, or discharging sinus overlying the joint.

Diagnosis of Prosthetic Arthritis

- ESR and C-reactive protein(CRP) may be high.
- Aspiration & surgical exploration to obtain specimen for culture & sensitivity testing & histopathology.
- Skin flora regarded as pathogens if isolated from multiple deep tissue cultures.
- Plain X-ray may not be helpful
- **Arthrography** may help define sinus tracts
- Bone scan-not specific for infection

Treatment & Management

- Surgical debridement and prolonged antimicrobial therapy
- Surgery: removal of prosthesis
- Antibiotic –impregnated cement during re-implantation
- Antimicrobial for 6 weeks:
- Begin empiric IV antibiotic to cover MRSA and Gram negative rods (Vancomycin+ Cefepime, Ciprofloxacin,or Aminoglycoside)
- Chronic therapy with oral drug if removal of prosthesis not possible.